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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/011,167	10/05/1998	JOHANNES J. GEUZE	RILE.001.OOU	9536

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BARBARA RAE VENTER
RAE VENTER LAW GROUP
PO BOX 60039
PALO ALTO, CA 943060039

EXAMINER	
DECLOUX, AMY M	
ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 02/07/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/011,167	Gueze And Mellef
Examiner	**Art Unit**
DeCloux, Amy	1644

-- The MAILING DATE of this communication appears on th cover sheet with the correspondenc address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on Dec 3, 2001

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) 2-4, 6, and 9-13 is/are pending in the applica

4a) Of the above, claim(s) 9-12 is/are withdrawn from considera

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) 2-4, 6, and 13 is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirem

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☒ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
18) ☐ Interview Summary (PTO-413) Paper No(s). _____
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other:

DETAILED ACTION

1. In view of the appeal brief filed on 12-3-01, PROSECUTION IS HEREBY REOPENED. A new grounds of rejection is set forth below.

To avoid abandonment of the application, appellant must exercise one of the following two options:

(a) file a reply under 37 CFR 1.111 (if this Office action is non-final) or a reply under 37 CFR 1.113 (if this Office action is final); or,

(b) request reinstatement of the appeal.

If reinstatement of the appeal is requested, such request must be accompanied by a supplemental appeal brief, but no new amendments, affidavits (37 CFR 1.130, 1.131 or 1.132) or other evidence are permitted. See 37 CFR 1.193(b)(2).

Claims 2-4, 6 and 13 are presently under consideration. None of applicant's after-final amendments, filed 4-23-01, 7-20-01 and 12-2-01, have been entered, in part due to the conflicting nature of the after-final amendments. It is noted that the instant office action is non-final.

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 13, 2, 3, 4 and 6 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an antigen presenting vesicle comprising a membrane and a MHC Class II protein wherein said antigen presenting vesicle is obtainable from an antigen presenting cell, does not reasonably provide enablement for an antigen presenting vesicle comprising a membrane and any MHC Class I protein, or any functional derivative or fragment thereof, wherein said antigen presenting vesicle is obtainable from any cell The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir.1988)). The factors most relevant to this rejection are the scope of the claims, the amount of direction or guidance provided, the lack of sufficient working examples, the unpredictability in the art and the amount of experimentation

required to enable one of skill in the art to practice the claimed invention. The specification is insufficient to enable one skilled in the art to practice the invention as broadly claimed without an undue amount of experimentation.

Claims 3-4, 6 and 13 are drawn to an antigen presenting vesicle comprising a membrane and a MHC Class I protein wherein said antigen presenting vesicle is obtainable from a cell, while claim 2 is drawn to an antigen presenting vesicle comprising a membrane and a MHC Class I or Class II protein wherein said antigen presenting vesicle is obtainable from a cell. The instant specification discloses in its examples, an antigen presenting vesicle derived from B cells only. There is insufficient guidance and direction in the instant specification and the prior art regarding an antigen presenting vesicle from any cell, as evidenced by Janeway et al (Immunobiology 3rd Edition) who teaches that antigens are presented by a limited number of cell types see page 7:15. Janeway also teaches on page 4:11 (Immunobiology 3rd Edition) that the function of MHC Class II molecules is to present peptides generated in the intracellular vesicles of B cells, macrophages and other antigen presenting cells to CD4 T cells. Therefore, it is not routine in the art to isolate antigen presenting vesicles from cells other than antigen presenting cells. Without more guidance and direction from the instant specification, it would require undue experimentation by one of ordinary skill in the art to predict from which cell the recited vesicles can be obtained.

There is insufficient guidance and direction in the instant specification and the prior art regarding the recited antigen presenting vesicles which comprise MHC Class I alone, as evidenced by Zitvogel et al (Nature Medicine 4(5):594-600, May 1998 who teaches that the potential advantages of exosomes in immunotherapy is due to its high levels of peptide bound MHC Class I and Class II molecules (see last paragraph of article) and therefore, the existence of the claimed vesicles with only class I and not class II molecules is not evident, and the efficacy of the claimed vesicles with only class I and not class II molecules in immunotherapy, as asserted in the instant specification, is not clear. Without more guidance and direction from the instant specification, it would require undue experimentation by one of ordinary skill in the art to make and use the recited vesicles comprising class I and not class II molecules.

There is insufficient guidance and direction in the instant specification and the prior art regarding the isolation of the recited antigen presenting vesicles which comprise a functional derivative or fragment thereof of a MHC Class I protein, as native cells do not routinely produce vesicles with fragments or derivatives of MHC proteins, and because the instant specification neither defines nor describes a functional derivative or fragment thereof of a MHC Class I protein and the prior art does not teach a vesicle

comprising a a functional derivative or fragment thereof of a MHC Class I protein . Without more guidance and direction from the instant specification, it would require undue experimentation by one of ordinary skill in the art to make and use the recited vesicle comprising a functional derivative or fragment thereof, of a MHC Class I protein.

In re Fisher, 166 USPQ 18 indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. In view of the quantity of experimentation necessary, the limited working examples, the unpredictability of the art, the lack of sufficient guidance in the specification and the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

4. Claims 13, 2, 3, 4 and 6 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

The specification does not reasonably provide a **written description** of an antigen presenting vesicle comprising a membrane and any MHC Class I protein, or any functional derivative or fragment thereof, nor of an antigen presenting vesicle obtainable from any cell other than an antigen presenting cell.

The instant specification provides insufficient description of cells other than antigen presenting cells from which the recited vesicles would be obtainable. The instant specification discloses in its examples, an antigen presenting vesicle derived from B cells only, and Janeway et al (Immunobiology 3rd Edition) who teaches that antigens are presented by a limited number of cell types see page 7:15. Therefore, one of ordinary skill would not know if one was in possession of a cell type from which the recited vesicle could be obtainable without a further description of the cells in the instant specification.

The instant specification provides insufficient description of antigen presenting vesicles which comprise a functional derivative or fragment thereof of a MHC Class I protein because the instant specification neither defines nor describes a functional derivative or fragment thereof of a MHC Class I protein and the prior art does not teach such a vesicle. Therefore, one of ordinary skill would not know if one was in possession of the recited vesicle comprising a functional derivative or fragment thereof, of a MHC Class I protein without a further description of the vesicle in the instant specification

Applicant is directed to the Revised Interim Guidelines for the

Examination of Patent Applications Under the 35 U.S.C. 112, 1st "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

5. The following is a quotation of the second paragraph of 35 U.S.C.112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the Applicant regards as his invention.

Claims 2-4, 6 and 13 are rejected under *35 U.S.C. § 112*, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

A) Claim 2 is indefinite because the recited phrase " said major histocompatibility complex protein " lacks antecedent basis in claim 13. It is noted that claim 13 recites "a major histocompatibility complex (MHC) class I protein or a functional derivative or fragment thereof. Therefore, it is noted that Claim 13 does not encompass a major histocompatibility complex protein derived from MHC Class II.

B) Claim 6 is indefinite because the recited phrase "wherein said antigen presenting cell" lacks antecedent basis in claim 13.

C) Claims 2-4, 6 and 13 are indefinite in the recitation of the phrase "or fragment thereof" in line 3 of claim 13, because it is not clear whether said phrase modifies the term "derivative" or the phrase "class I protein" or both.

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 13, 2, 3, 4 and 6 are rejected under 35 U.S.C. § 102(b) as being anticipated by Harding and Gueze (J. Immunology, 151:3988-3998, 1993), as evidenced by Zitvogel et al (Nature Medicine 4(5):594-600, May 1998.

Harding and Gueze teach the subcellular fractionation of murine peritoneal macrophages to produce fractions containing MHC Class II molecules (see entire article, especially page 3990, column 2, last 2 paragraphs), and that fractions containing lysozymes and light density membranes contained peptide-MHC-II complexes that were detected by T cells, (see entire article especially page 3992, column 1, last paragraph). Claims 13, 3, 4 and 6 are included in the instant rejection because Zitvogel et al teach that human monocyte derived multivesicular MIICs contain abundant MHC class I molecules (see entire article, especially page 594, column 2). Because the isolation of the vesicles taught by Harding and Gueze and those taught by Zitvogel et al., were isolated in a similar fashion, one would expect the vesicles taught by Harding and Gueze to display identical properties as those taught by Zitvogel. Therefore, the vesicles taught by Harding and Gueze inherently contain MHC Class I molecules, as well as class II molecules. Since the Office is not equipped to manufacture the claimed fusion protein and/or the referenced fusion protein, nor to conduct comparisons, the burden is on the applicant to establish a patentable distinction between the claimed and referenced fusion proteins. See In re Best, 195 USPQ 430, 433 (CCPA 1977).

Therefore, the referenced teachings anticipate the claimed references.

8.. Claims 13, 2, 3, 4 and 6 are rejected under 35 U.S.C. § 102(b) as being anticipated by Amigorena et al (Nature, 369:113-120, 1994)as evidenced by Zitvogel et al (Nature Medicine 4(5):594-600, May 1998.

Amigorena et al teach the subcellular fractionation of a B cell line to produce fractions containing membrane vesicles with MHC Class II molecules (see entire article, especially page 114, column 2, last paragraph), which contained processed peptide (see entire article, especially page 118, first paragraph of the Discussion Section). Claims 13, 3, 4 and 6 are included in the instant rejection because Zitvogel et al teach that human monocyte derived multivesicular MIICs contain abundant MHC class I molecules (see entire article, especially page 594, column 2). Because the isolation of the vesicles taught by Amigorena et al. and those taught by Zitvogel et al., were isolated in a similar fashion, (see the Materials and Methods sections of both references) one would expect the vesicles taught Amigorena et al to display identical properties as those taught by Zitvogel. Therefore the vesicles taught by Amigorena et al inherently contain MHC Class I molecules, as well as class II molecules. Since the Office is not equipped to manufacture the claimed fusion protein and/or the referenced fusion protein, nor to conduct comparisons, the burden is on the applicant to

establish a patentable distinction between the claimed and referenced fusion proteins. See In re Best, 195 USPQ 430, 433 (CCPA 1977).

Therefore, the referenced teachings anticipate the claimed references.

9. No claim is allowed.

Note: Formal drawings and/or photographs have been submitted which fail to comply with 37 CFR 1.84. Please see the form PTO-948 enclosed with Paper No.13, mailed 8-14-00.

As of May 3, 2001, examiners may not permit corrections to drawings to be held in abeyance. Applicant must submit proposed drawing corrections in response to the requirement

INFORMATION ON HOW TO EFFECT DRAWING CHANGES

1. Correction of Informalities -- 37 CFR 1.85

New corrected drawings must be filed with the changes incorporated therein. Identifying indicia, if provided, should include the title of the invention, inventor's name, and application number, or docket number (if any) if an application number has not been assigned to the application. If this information is provided, it must be placed on the front of each sheet and centered within the top margin. Applicant is required to submit acceptable corrected drawings within the time period set in the Office action. See 37 CFR 1.85(a). Failure to take corrective action within the set period will result in **ABANDONMENT** of the application.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amy DeCloux whose telephone number is (703) 306-5821. The examiner can normally be reached Monday through Friday from 9:00 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Amy DeCloux, Ph.D. Patent Examiner,
Group 1640, Technology Center 1600
February 5, 2002

David a Saunders

DAVID SAUNDERS
PRIMARY EXAMINER
ART UNIT ~~182~~ 1644